Attorney's Docket No.: 0119378-00560 / 4207

Applicant: Hamann et al. **RCE & Preliminary Amendment** Serial No.: 10/712,456

: November 13, 2003 Filed

AMENDMENTS TO THE CLAIMS:

Claims 1, 4-8 and 10-19 are pending. Please amend claim 1, 4-8 and 11-19 as indicated below. This listing of claims replaces all prior versions and listings of claims in the application.

LISTING OF CLAIMS:

(Currently amended) A compound of the formula I 1.

$$R_{2}$$
 R_{2}
 N
 X
 X

or a pharmaceutically acceptable salt thereof, wherein:

- is selected from the group consisting of alkyl or substituted alkyl, alkenyl or R_1 substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, and CH₂OR₄;
- is selected from the group consisting of hydrogen, alkyl or substituted alkyl, R_2 alkenyl or substituted alkenyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heterocycle or substituted heterocycle, heteroaryl or substituted heteroaryl and CH₂OR₄;
- is selected from the group consisting of hydrogen, alkyl or substituted alkyl, R_3 CH₂OR₄, OR₂, SR₂, halo, NHR₂, NHCOR₄, and NHCONR₄R₄;
- for each occurrence are each independently selected from the group consisting R₄ and R₄' of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heterocyclo or substituted heterocyclo and heteroaryl or substituted heteroaryl;
 - G is selected from the group of:

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 R_9 R_8 R_8 R_8 R_8 R_{10} R_{11} R_{11}

wherein:

 R_8 is CN;

R₉, R₁₀, and R₁₁ are each independently selected from the group consisting of hydrogen (H), NO₂, CN, CF₃, OR₄, CO₂R₄, NR₄R₄', CONR₄R₄', CH₂OR₄, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteroaryl;

A to F are each independently is selected from among N and CR₁;

J, K, L, P, and Q are each independently is selected from among NR_{12} , O, S, SO, SO₂ or $CR_{12}R_{12}$ ';

 R_{12} and R_{12} ' in each functional group are each independently selected from a bond or R_1 ; m is an integer of 0 or 1;

X is a linking group selected from the group consisting of NR₄ and CHR₄;

Y is selected from the group consisting of O, NR₄, NOR₄, S and CH₂; and

Z is -O- or NR_4 ;

with the following provisos:

- (a) when Y is NOR₄, R₄ is not hydrogen;
- (b) when R₁ is methyl,

 X is NH, [[;]] and

 Y is O or S, then

 Z is not O;
- (c) when (i) R_1 is methyl,
 - (ii) X is NH,
 - (iii) Y is NR₄,

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(iv) R₄ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteroaryl, and

(v) G has the following structure:

wherein:

R₁₃ is selected from the group consisting of hydrogen, cyano (-CN), nitro (-NO₂), halo, heterocyclo, OR₁₄, CO₂R₁₅, CONHR₁₅, COR₁₅, S(O)_pR₁₅, SO₂NR₁₅NR₁₅', NHCOR₁₅ and NHSO₂R₁₅;

R₁₄ in each functional group is independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, CHF₂, CF₃ and COR₁₅;

R₁₅ and R₁₅' in each functional group are each independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, heterocycloalkyl or substituted heterocycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heteroaryl or substituted heteroaryl and -CN;

AA and BB are each independently is selected from the group consisting of hydrogen, halo, cyano (-CN), nitro (-NO₂), alkyl or substituted alkyl and OR₁₄; and

p is an integer from 0 to 2,

then Z is not O.

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2. (Cancelled).

- 3. (Cancelled).
- 4. (Currently amended) The compound as defined in of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

 R_1 is alkyl;

R₂ is hydrogen or alkyl;

R₃ is hydroxyl;

Y is O; and

Z is O.

- 5. (Currently amended) A pharmaceutical composition, comprising: a compound or salt as defined in of claim 1; and a pharmaceutically acceptable carrier therefor.
- 6. (Currently amended) The pharmaceutical composition as defined in of claim 5, further comprising a growth promoting agent.
- 7. (Currently amended) A pharmaceutical composition, comprising:
 a compound as defined in of claim 1, or a pharmaceutically acceptable salt thereof, and
 at least one additional therapeutic agent selected from the group consisting of
 parathyroid hormone, bisphosphonates, estrogen, testosterone, progesterone, selective
 estrogen receptor modulators, growth hormone secretagogues, growth hormone, progesterone
 receptor modulators, anti-diabetic agents, anti-hypertensive agents, anti-inflammatory agents,
 anti-depressants, anti-obesity agents, cardiac glycosides, cholesterol lowering agents,
 anti-depressants, anti-anxiety agents, anabolic agents, and thyroid mimetics.
- 8. (Currently amended) A method for treating prostate cancer, <u>comprising</u>: which comprises administering to a mammalian species in need of treatment an effective amount of a compound as <u>defined in of claim 1</u> or a pharmaceutically acceptable salt thereof.
 - 9 (Cancelled).
- 10. (Previously presented) A compound selected from the group consisting of 1-(4-Cyano-2-ethyl-3-(trifluoromethyl)phenyl-1-carbamoyl)-3-hydroxy-pyrrolidine-2-carboxylic acid or a pharmaceutically acceptable salt thereof;
- 1-(4-Cyanonaphthalen-1-ylcarbamoyl-3-hydroxy-pyrrolidine-2-carboxylic acid methyl ester or a pharmaceutically acceptable salt thereof;

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1-(5-Chloro-6-cyano-pyridin-3-ylcarbamoyl)-3-hydroxypyrrolidine-2-carboxylic acid methyl ester or a pharmaceutically acceptable salt thereof; and

1-[2-(4-Cyanonaphthalen-1-yl)acetyl]-3-hydroxypyrrolidine-2-carboxylic acid methyl ester or a pharmaceutically acceptable salt thereof.

11. (Currently amended) A pharmaceutical composition, comprising:
a compound as defined in of claim 10, or a pharmaceutically acceptable salt thereof;
[[,]] and a pharmaceutically acceptable carrier therefor.

- 12. (Currently amended) The pharmaceutical composition as defined in of claim 11, further comprising a growth promoting agent.
- 13. (Currently amended) A pharmaceutical composition, comprising:
 a compound as defined in of claim 10, or a pharmaceutically acceptable salt thereof;
 [[,]] and

at least one additional therapeutic agent selected from the group consisting of parathyroid hormone, bisphosphonates, estrogen, testosterone, progesterone, selective estrogen receptor modulators, growth hormone secretagogues, growth hormone, progesterone receptor modulators, anti-diabetic agents, anti-hypertensive agents, anti-inflammatory agents, antiosteoporosis agents, anti-obesity agents, cardiac glycosides, cholesterol lowering agents, anti-depressants, anti-anxiety agents, anabolic agents, and thyroid mimetics.

- 14. (Currently amended) A method for treating prostate cancer, comprising: which comprises administering to a mammalian species in need of treatment an effective amount of a compound as defined in of claim 10 or a pharmaceutically acceptable salt thereof.
 - 15. (Currently amended) A compound of formula I

$$R_{2}$$
 R_{2}
 R_{3}
 R_{3}
 R_{3}
 R_{3}
 R_{3}
 R_{3}
 R_{3}
 R_{3}
 R_{3}

or a pharmaceutically acceptable salt thereof, wherein:

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R₁ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, and CH₂OR₄;

- R₂ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heterocyclo or substituted heterocyclo, heteroaryl or substituted heteroaryl and CH₂OR₄;
- R₃ <u>is</u> selected from the group consisting of alkyl or substituted alkyl, and CH₂OR₄;
- R₄ and R₄' for each occurrence are each independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heterocyclo or substituted heterocyclo and heteroaryl or substituted heteroaryl;
 - G is selected from the group consisting of:

$$R_9$$
 R_8
 R_8
 R_8
 R_8
 R_8
 R_8
 R_8
 R_8
 R_8
 R_{10}
 R_{11}
 R_{11}

wherein:

R₈ is CN;

R₉, R₁₀, and R₁₁ are each independently selected from the group consisting of hydrogen (H), NO₂, CN, CF₃, OR₄, CO₂R₄, NR₄R₄', CONR₄R₄', CH₂OR₄, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteroaryl;

A to F are each independently is selected from among N and CR₁;

J, K, L, P, and Q are each independently is selected from among NR_{12} , O, S, SO, SO₂ or $CR_{12}R_{12}$ ';

 R_{12} and R_{12}^{\prime} in each functional group are each independently selected from a bond or R_1 ;

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m is an integer of 0 or 1;

X is a linking group selected from the group consisting of NR₄ and CHR₄;

Y is selected from the group consisting of O, NR₄, NOR₄, S and CH₂; and

Z is -O- or NR_4 ;

with the following provisos:

(a) when Y is NOR₄, R₄ is not hydrogen;

- (b) when R_1 is methyl, X is NH, and Y is O or S, then Z is not O;
- (c) when
 - (i) R_1 is methyl,
 - (ii) X is NH,
 - (iii) Y is NR₄,
 - (iv) R₄ is selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, cycloalkyl or substituted cycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, and heteroaryl or substituted heteroaryl, and
 - (v) G has the following structure:

wherein:

R₁₃ is selected from the group consisting of hydrogen, cyano (-CN), nitro (-NO₂), halo, heterocyclo, OR₁₄, CO₂R₁₅, CONHR₁₅, COR₁₅, S(O)_pR₁₅, SO₂NR₁₅NR₁₅', NHCOR₁₅ and NHSO₂R₁₅;

R₁₄ in each functional group is independently is selected from the group consisting of hydrogen, alkyl or substituted alkyl, CHF₂, CF₃ and COR₁₅;

R₁₅ and R₁₅' in each functional group are each independently selected from the group consisting of hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkynyl or

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substituted alkynyl, cycloalkyl or substituted cycloalkyl, heterocycloalkyl or substituted heterocycloalkyl, arylalkyl or substituted arylalkyl, aryl or substituted aryl, heteroaryl or substituted heteroaryl and CN;

AA and BB are each independently is selected from the group consisting of hydrogen, halo, cyano (-CN), nitro (-NO₂), alkyl or substituted alkyl and OR₁₄; and

p is an integer from 0 to 2,

then Z is not O.

16. (Currently amended) A pharmaceutical composition, comprising:
 a compound as defined in of claim 15, or a pharmaceutically acceptable salt thereof;
 [[,]] and

a pharmaceutically acceptable carrier therefor.

- 17. (Currently amended) The pharmaceutical composition as defined in of claim 16, further comprising a growth promoting agent.
- 18. (Currently amended) A pharmaceutical composition, comprising:
 a compound as defined in of claim 15, or a pharmaceutically acceptable salt thereof;
 [[,]] and

at least one additional therapeutic agent selected from the group consisting of parathyroid hormone, bisphosphonates, estrogen, testosterone, progesterone, selective estrogen receptor modulators, growth hormone secretagogues, growth hormone, progesterone receptor modulators, anti-diabetic agents, anti-hypertensive agents, anti-inflammatory agents, antiosteoporosis agents, anti-obesity agents, cardiac glycosides, cholesterol lowering agents, anti-depressants, anti-anxiety agents, anabolic agents, and thyroid mimetics.

19. (Currently amended) A method for treating prostate cancer, comprising:

which comprises administering to a mammalian species in need of treatment an

effective amount of a compound as defined in of claim 15 or a pharmaceutically acceptable
salt thereof.